P<0.05); sixteen-week-old: heart rate (403±15 *VS* 347±19 (beats/min), P<0.05), blood pressure: (206±11/141±16 *VS* 119±6/77±11 mmHg, P<0.05). Second, catestatin could cause short-term heart rate decline of SHR, (416±29 *VS* 371±15(beats/min), P<0.05), but still higher than WKY levels, (371±15 *VS* 326±25(beats/min), P<0.05). Catestatin long-term supplement had no effect on heart rate of SHR, (408±64 *VS* 403±15 (beats/min), P=0.896). Third, whether short or long term, catestatin had no effect on blood pressure of SHR, short-term (195±3/150±12 *VS* 194±5/145±12mmHg, P>0.05), long-term(216±19 /177±13 *VS* 206±11/162±10 mmHg, P>0.05).

CONCLUSIONS In addition to increased blood pressure, heart rate of SHR is also higher than WKY, indicating the presence of significant sympathetic activation of hypertension. Catestatin can lower heart rate in hypertension transiently, but long-term supplement does not affect heart rate, there may be other compensatory mechanisms. Catestatin does not also affect blood pressure in hypertension. These conclusions indicate catestatin may inhibit the sympathetic activation in hypertension to some extent, and involve in the pathogenesis of hypertension, but not be the deciding factor.

GW26-e4750

Autophagy Inhibits High Glucose Induced Cardiac Microvascular Endothelial Cells Apoptosis by mTOR Signal Pathway

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OBJECTIVES Cardiac microvascular endothelial cells (CMECs) dysfunction is an important pathophysiological event in the cardiovascular complications induced by diabetes. However, the underlying mechanism is not fully clarified. Autophagy is involved in programmed cell death. Here we investigated the potential role of autophagy on the CMECs injury induced by high glucose.

METHODS CMECs were cultured in normal or high glucose medium for 6h, 12h and 24h respectively. The autophagy of CMECs was measured by green fluorescence protein (GFP)-LC3 plasmid transfection. Moreover, the apoptosis of CMEC was determined by flow cytometry. Furthermore, 3-Methyladenine (3MA), ATG7 siRNA and rapamycin were administrated to regulate the autophagy state. Moreover, Western blotting assay was performed to measure the expressions of Akt, mTOR, LC3 and p62.

RESULTS High glucose stress decreased the autophagy, whereas increased the apoptosis in CMECs time dependently. Meanwhile, high glucose stress activated the Akt/mTOR signal pathway. Furthermore, autophagy inhibitor, 3-MA and ATG7siRNA impaired the autoghagy and increased the apoptosis in CMECs induced by high glucose stress. Conversely, rapamycin up-regulated the autophagy and decreased the apoptosis in CMECs under high glucose condition.

CONCLUSIONS Our data suggested that autophagy, as an adaptive response, is directly inhibited by high glucose in CMECs. Furthermore, the autophagy was mediated, at least in part, by mTOR signaling.

GW26-e4765

Vasomotor effect of salidroside on acute exhaustive rat mesenteric artery and its calcium regulation mechanisms

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OBJECTIVES To investigate vasomotor effect of salidroside (SAL) on acute exhaustive rat mesenteric artery, and to explore its calcium regulation mechanisms.

METHODS Tension was measured by DMT 620M system to evaluate the vasomotor effect of SAL on acute exhaustive rat mesenteric artery rings, and acetylcholine (ACh), N-nitro-L-arginine methylester (L-NAME), an inhibitor of nitric oxide synthase (NOS), calcium deprivation and calcium addition were used. Besides, for protein assay, 40 adult male Sprague Dawley SD rats were randomly divided into control group (Con), salidroside group (SAL), acute exhaustive swimming group (EE) and salidroside-acute exhaustive swimming group (SE). The protein expression of IP3R1 and RyR2 were determined by Western blotting.

RESULTS ①AS acetylcholine (ACh ($1\mu mol\cdot L^{-1}$)) acted on acute exhaustive rat mesenteric artery precontracted by phenylephrine (PE ($1\mu mol\cdot L^{-1}$)), Vasodilation rate of vascular was 84.90% ± 11.42%, which suggested that acute exhaustive rat mesenteric vascular endothelial injury was not obvious. ②SAL ($10^{-8} mol\cdot L^{-1}$ - 10^{-4} $mol\cdot L^{-1}$) had significantly relaxant effect on exhaustive mesenteric aortic rings pre-incubated by L-NAME ($0.1mmol\cdot L^{-1}$) for 20 min, and then pre-contracted by PE ($1\mu mol\cdot L^{-1}$) ($P<0.01$ in 10^{-4} $mol\cdot L^{-1}$ SAL). ③With calcium deprivation and calcium addition, SAL relaxed endothelium-denuded mesenteric artery precontracted by PE ($1\mu mol\cdot L^{-1}$) ($P<0.01$ in 10^{-5} $mol\cdot L^{-1}$ SAL), while SAL had no effect on the increasing tension of mesenteric artery induced by adding $CaCl_2$ ($P>0.05$). ④In exhaustive swimming group the expression of IP_3R1 and RyR2 were bothinhibited ($P<0.01$), While in salidroside group and salidroside-acute exhaustive swimming group, SAL significantly reduced the expression of IP_3R1, and increased the expression of RyR2 ($P<0.01$).

CONCLUSIONS These results indicate that acute exhaustive rat mesenteric artery keeps relaxant state which might be associated with compensatory autoregulation. Moreover, the dominated effect of SAL on acute exhaustive rat mesenteric artery is to relax vessels which is related to inhibiting the expression of IP_3R1 and then suppressing intracellular calcium release and possibly not related to influx of extracellular calcium.

GW26-e1362

Activation of Cannabinoid Receptor 2 improves therapeutic efficacy of Adipose-Derived Mesenchymal Stem Cells to alleviate myocardial ischemia injury through AMPK/SIRT1 and TLR4/NF-κB Signaling Pathways

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OBJECTIVES Clinical application of cellular therapy for cardiac regeneration is significantly hampered by the low retention of engrafted cells, which is mainly attributable to the poor microenvironment dominated by inflammation and oxidative stress in the host's infarcted myocardium. This study aims at investigating whether Cannabinoid Receptor 2 (CB2R) agonist AM1241 will improve survival of adipose-derived mesenchymal stem cells (AD-MSCs) after transplantation into infarcted hearts and further discussed its underlying mechanisms.

METHODS We investigated the therapeutic effects of Cannabinoid Receptor 2 (CB2R) agonist AM1241 and co-transplantation of MSCs on cardiac repair in myocardial infarction by using bioluminensence imaging. AD-MSCs were isolated from Fluc+-eGFP+ transgenic mice (Tg [Fluc- egfp]). Animals were divided into 7 groups: (1) Sham group, (2) MI+PBS group, (3) MI+CB2R agonist AM1241 group, (4) MI+AD-MSCs group, (5) MI+AD-MSCs+ CB2R agonist AM1241 pretreatment before transplantation group, (6) MI+AD-MSCs transfected with SIRT1 siRNA+ CB2R agonist AM1241, and (7) MI+AD-MSCs+ CB2R agonist AM1241 group. Cardiac performance was then quantified by echocardiography as well as molecular and pathologic analysis of heart samples at serial time points. The survival and engraftment of transplanted MSCs were also assessed by both bioluminensence imaging and histologic analysis. To reveal possible mechanisms, AD-MSCs were subjected to hypoxia/serum deprivation (H/SD) injury to simulate ischemic conditions in vivo. Western blot assay was used to detect the expression of related signal transduction proteins in inflammation and oxidative stress.

RESULTS Noninvasive in vivo bioluminescence imaging and histological staining showed that Cannabinoid Receptor 2 (CB2R) agonist AM1241 improved the retention and survival of intramyocardially injected AD-MSCs. Moreover, combined therapy of CB2R agonist and AD-MSCs inhibited host cardiomyocyte apoptosis, reduced fibrosis, and improved cardiac function and angiogenesis, while it concomitantly decreased inflammatory cytokines (e.g., tumor necrosis factor-a and interleukin-1β) and increased growth factor (e.g., vascular endothelial growth factor and basic fibroblast growth factor) expression in infarct myocardium. In AD-MSCs subjected to H/SD injury, CB2R agonist AM1241 (5μM) improved AD-MSCs survival under H/SD condition. Western blot revealed that the CB2R agonist enhanced Adenosine 5'-monophosphate (AMP)-activated protein kinase (AMPK) phosphorylation, SIRT1 expression, which resulted in reduced TLR4, TRAF-6, and MyD88 protein expression, inhibited IκBαphosphorylation and NF-κB-p65 nuclear translocation.

CONCLUSIONS CB2R agonist can enhance the functional survival of transplanted AD-MSCs in infarcted myocardium, at least partially, via